

CLAIMS

We claim:

1. An isolated compound comprising an indirubin molecule substituted with a halogen at position C6 of the indirubin molecule.
2. The isolated compound of claim 1, wherein the compound inhibits GSK-3 activity with an IC_{50} value of less than 0.1 μM using GS-1 peptide as a substrate.
3. A pharmaceutically acceptable salt or solvate of the isolated compound of claim 1.
4. The isolated compound of claim 1, wherein the compound is selected from the group consisting of 6-bromoindirubin (5a), 6,6'-dibromoindirubin (12b), 6-bromoindirubin-3'-oxime ("BIO") (7a), 6,6'-dibromoindirubin-3'-oxime (13b), 6-bromoindirubin-3'-methoxime (9a), 6-bromo-5-methylindirubin (5f) and 6-bromoindirubin-3'-acetoxime (8a), and pharmaceutically acceptable salts thereof.
5. The isolated compound of claim 1, wherein the compound is selected from the group consisting of 6-bromo-5-aminoindirubin (27) and 6-bromo-5-amino-3'-oxime-indirubin (28) and pharmaceutically acceptable salts thereof.
6. A compound selected from the group of 6-bromoindirubin (5a), 6,6'-dibromoindirubin (12b), 6-bromoindirubin-3'-oxime ("BIO") (7a), 6,6'-dibromoindirubin-3'-oxime (13b), 6-bromoindirubin-3'-methoxime (9a), 6-bromo-5-methylindirubin (5f), 6-bromo-5-aminoindirubin (27), 6-bromo-5-amino-3'-oxime-indirubin (28), 6-bromoindirubin-3'-acetoxime (8a), 5-aminoindirubin (23), 5-amino-3'-oxime-indirubin (24) and pharmaceutically acceptable salts thereof.
7. An inhibitor of GSK-3 activity, wherein the inhibitor comprises an indirubin molecule with a halogen atom covalently attached to carbon number 6, and the inhibitor inhibits GSK-3 activity with an IC_{50} below 5 μM in an activity assay using GS-1 peptide as a substrate.
8. The inhibitor of claim 7, wherein the halogen atom is bromine.

9. A pharmaceutical composition comprising 6-bromoindirubin, or pharmaceutically acceptable salt thereof, and a pharmaceutically acceptable vehicle.
10. A method of inhibiting GSK-3 activity comprising contacting GSK-3 with the inhibitor of claim 7.
11. The method of claim 10, wherein the GSK-3 activity is inhibited *in vitro*.
12. The method of claim 10, wherein the GSK-3 activity is inhibited in a cell.
13. The method of claim 10, wherein the inhibitor is selected from group of compounds consisting of 6-bromoindirubin (5a), 6,6'-dibromoindirubin (12b), 6-bromoindirubin-3'-oxime (7a), 6,6'-dibromoindirubin-3'-oxime (13b), 6-bromoindirubin-3'-methoxime (9a), 6-bromoindirubin-3'-acetoxime (8a), 6-iodoindirubin (5c), 6-iodoindirubin-3'-oxime (7c) and 6-iodoindirubin-3'-acetoxime (8c), and pharmaceutically acceptable salts thereof.
14. The method of claim 10, wherein the inhibitor is selected from group of compounds consisting of 6-bromo-5-aminoindirubin (27), 6-bromo-5-amino-3'-oxime-indirubin (28), and pharmaceutically acceptable salts thereof.
15. A method for the isolation of 6-bromoindirubin from a natural source comprising the steps described in Example 6.1.2.
16. A method for preventing, treating or ameliorating type 2 diabetes or Alzheimer's disease in a mammal, comprising administering to the mammal an effective disease-treating or condition-treating amount of a pharmaceutical composition of indirubin-type compound consisting of 6-bromoindirubin (5a) or a 6-bromoindirubin derivative or analogue.